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Tadashi Okamoto

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EXAMINER

BHAT, NARAYAN KAMESHWAR

ART UNIT

PAPER NUMBER

1634

MAIL DATE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/518,559	<b>Applicant(s)</b> OKAMOTO, TADASHI	
	<b>Examiner</b> Narayan K. Bhat	<b>Art Unit</b> 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 18 June 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-38 is/are pending in the application.
- 4a) Of the above claim(s) 12, 16-23, 25, 26 and 36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11, 13-15, 24, 27-35, 37 and 38 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>12/21/2004</u> | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Claims 1-38 are pending in the application
2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in on December 21, 2004. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

### **Election/Restrictions**

3. Applicant's election without traverse of Group I, claims 1-11, 13-15, 24, 27-35 and 37-38, in the reply filed on March 21, 2007 is acknowledged. Applicant's election of species of formula II with traverse of Group I, claims 1-11, 13-15, 24, 27-35 and 37-38, in the reply filed on June 18, 2007 is acknowledged. The traversal is on the ground(s) that there is no serious burden on the Examiner to examine all of the claims in the present application particularly since the searches are co-extensive.

The species recited in the claims pending are three different formulae and each formula has a unique structure and not common to other. It would pose a serious burden on the examiner to search and examine all inventions because, a search indicating the formula II is known or would have been obvious would not extend to a holding that the formula I and III known or would have been obvious. Similarly a search for the invention of formula I and III would not be coextensive because a search indicating the formula I and III is novel or unobvious would not extend to a holding that

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the formula I is novel or unobvious. Therefore restriction for examination purposes as indicated is proper.

4. Claims 12, 16-23, 25-26 and 36 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on June 18, 2007.

5. Claims 1-11, 13-15, 24, 27-35 and 37-38 are under prosecution.

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-6, 13-15, 24, 27-30 and 37-38 are rejected under 35 U.S.C. 102(b) as being anticipated by O'Donnell et al (WO 98/20020 published May 14, 1998, herein after O'Donnell).

Regarding claim 1, O'Donnell teaches a method of acquiring data on the mass of a substance fixed on a substrate, that include photo cleavable linker moiety (pg. 33, lines 12-17) that is a structure including a partial structure to be disconnected by light to

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fix the substance on the substrate (pg. 33, 18-23); irradiating the substance fixed on the substrate with a laser (pg. 34, lines 26-28), that is light for inducing the disconnection of the partial structure to be disconnected by light; and analyzing the mass spectrum of the substance which is brought in an unfixed state by disconnecting the partial structure by the irradiation of light (Fig. 17, pg. 25 lines 7-29).

Regarding claim 2, O'Donnell teaches a method that include a means of analyzing the mass spectrum is matrix assisted laser desorption ionization time-of-flight mass spectrometry (pg. 49, lines 17-22).

Regarding claim 3, O'Donnell teaches a laser, i.e., light for inducing the disconnection of the partial structure to be disconnected by light is a laser beam used for the analysis by MALDI-TOF MS (pg. 34, lines 26-28),

Regarding claim 4, O'Donnell teaches that the laser beam used for the analysis by MALDI-TOF MS is a nitrogen laser beam (pg. 73, line 7).

Regarding claim 5, O'Donnell teaches that the substance fixed on the substrate is nucleic acid (pg. 72, lines 20-22).

Regarding claim 6, O'Donnell teaches that the substance a structure containing nitrobenzene is selected as the partial structure to be disconnected by the irradiation of light (pg. 33, lines 12-17).

Regarding claim 13, O'Donnell teaches a substance (matrix substance) for assisting the desorption and ionization of the substance fixed on the substrate is applied to at least a region to be used for the mass spectrometry of the substrate (pg.81, lines 25-29).

Regarding claim 14, O'Donnell teaches the thickness of the coating film of the matrix substance is large enough and required for the desorption and ionization of the substance fixed on the substrate (Fig. 12, pg. 85, lines 20-29).

Regarding claim 15, O'Donnell teaches a method of acquiring data on the mass of a bio-related substance on each matrix of a biochip having a plurality of bio-related substances fixed on a substrate in a matrix form by a structure including a partial structure to be disconnected by light, the method comprising the steps of: irradiating the bio-related substance on each matrix fixed on the substrate with a laser (pg. 34, lines 26-28) that is a light for inducing the disconnection of the partial structure to be disconnected by light; and analyzing the mass spectrum of the bio-related substance which is brought in an unfixed state by disconnecting the partial structure by the irradiation of light (Fig. 16-18, pg. 25, lines 7-29, pg. Example 5).

Regarding claim 24, O'Donnell teaches method of acquiring data on the mass of a bio-related substance on each matrix of a biochip having a plurality of bio-related substances fixed on a substrate in a matrix form and the mass of a substance which interacts with the bio-related substance, the method comprising the steps of: fixing the bio-related substance on each matrix on the substrate by photo cleavable linker (pg. 33, lines 12-17), that is a structure including a partial structure to be disconnected by light; placing the substance which interacts with the bio-related substance on each matrix of the biochip under an interactive condition (pg. 81, lines 25-29; See the entire sample preparation and dispensing section); irradiating the bio-related substance fixed on the substrate with a laser (pg. 34, lines 26-28), that is a light for inducing the disconnection of the partial structure to be disconnected by light; and analyzing the mass spectra of the bio-related substance which has been brought in an unfixed state by the irradiation of light and the substance which has interacted with the bio-related substance in an unfixed state at the same time by disconnecting the partial structure (Figs. 16-18, pg. 25, lines 7-29; Example 5).

Regarding claim 27, O'Donnell teaches a method of determining a base sequence of nucleic acid, comprising the steps of: (1) fixing, to a substrate, nucleic acid (DNA) complementary to a part or an entire part of a base sequence on a 3'-side from a site desired for analysis of a base sequence of nucleic acid (DNA) desired for analysis of the base sequence as a primer used for performing an enzymatic nucleic acid extension reaction, using the nucleic acid desired for analysis of the base sequence as

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a template, in a structure containing a partial structure to be disconnected by light on a 5'-side from the complimentary base sequence in the primer (Figs. 18 and 19, pg. 25 and 26, lines 24-29 and 1-22); (2) annealing the nucleic acid desired for analysis of the base sequence to the primer fixed to the substrate at the complementary base sequence portion to form a hybrid (Fig. 18, top left panel) ; (3) performing the enzymatic extension reaction using the nucleic acid desired for analysis of the base sequence as a template, on the substrate where the hybrid is formed, in the presence of appropriate amounts of 4 kinds of 2'-deoxynucleotide triphosphate (dNTP: N is A; adenine, G; guanine, C; cytosine, T; thymine) required for the enzymatic nucleic acid extension reaction and the 4 kinds of 2',3'-dideoxynucleotide triphosphate (ddNTP) as a terminator for an extension reaction (Fig. 18, Top left panel, see the step probe with ddT, pg. 26, lines 1-8 )

O'Donnell also teaches removing the template nucleic acid from the substrate where the extension reaction is effected (pg. 37, lines 1-20, step 4 of the said claim) and further teaches irradiating a plurality of extension reaction products having different chain lengths including a primer portion fixed to the substrate (Fig. 19).

O'Donnell also teaches photo cleavable linker moiety (pg. 33, lines 12-17) that is a structure containing a partial structure to be disconnected by a laser (pg. 34, lines 26-28), that is light, for disconnecting the partial structure to be disconnected, analyzing a molecular weight of the extension product disconnected by the irradiation with light by a MALDI-TOF MS method, and clarifying a base sequence of an extension portion of the extension product based on an increase in a molecular weight from a molecular weight



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of the primer in the extension product (Fig. 20, pg. 26, lines 24-29, step 5 of the said claim ; and (6) analyzing a part or an entire part of the base sequence desired for analysis of nucleic acid desired for analysis of the base sequence, based on the base sequence of the extension portion (Example 6 and 7, pg. 91-93) .

Regarding claim 28, O'Donnell teaches a laser, i.e., light for inducing the disconnection of the partial structure to be disconnected by light is a laser beam used for the analysis by MALDI-TOF MS (pg. 34, lines 26-28),

Regarding claim 29, O'Donnell teaches that the laser beam used for the analysis by MALDI-TOF MS is a nitrogen laser beam (pg. 73, line 7).

Regarding claim 30, O'Donnell teaches that the substance a structure containing nitrobenzene is selected as the partial structure to be disconnected by the irradiation of light (pg. 33, lines 12-17).

Regarding claim 37, O'Donnell teaches a Thermo sequenase, an enzyme used for the extension reaction has inherently heat resisting property (Fig. 19, pg. 92, lines 1-3).

Regarding claim 38, O'Donnell teaches a method wherein the substrate to which the primer is fixed is in a form of a nucleic acid chip in which a plurality of primer nucleic

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acids are placed in a matrix in the process (Fig. 19, pg. 83, lines 1-15) a part or an entire part of the primer nucleic acid is subjected to an enzymatic nucleic acid extension reaction together with the template thereof on the nucleic acid chip, and in the process (4), the matrix portion subjected to the extension reaction is analyzed by the MALDI-TOF MS method (pg. 83, lines 16-24).

### ***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 1, 6-11, 27 and 31-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Donnell et al (WO 98/20020 published May 14, 1998, herein after O'Donnell) in view of Heckman et al (USPN 6,124,099 issued September 26, 2000, herein after Heckman).

Claim 7 is dependent on claim 6, which is dependent on claim 1. Claim 8 is dependent on claim 7, which is dependent on claim 6, which is dependent on claim 1. Claim 9 is dependent on claim 8, which is dependent on claim 7, which is dependent on claim 6, which is dependent on claim 1. Claim 10 is dependent on claim 7, which is dependent on claim 6, which is dependent on claim 1. Claim 11 is dependent on claim 10, which is dependent on claim 7, which is dependent on claim 6, which is dependent

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on claim 1. Teachings of O'Donnell regarding claims 1 and 6 are described previously in this office action on pages 3-5.

Regarding claim 7, O'Donnell teaches an exemplary photocleavable cross-linker include but are not limited to, 3-amino-(2-nitrophenyl) propionic acid (pg. 33, line 15, pgs. 38-47) but do not teach specifically a photo cross linker containing a nitrobenzene derivative- succinimidyl 6-(4-bromomethyl-3-nitrobenzoyl) aminohexanoate (see instant specification paragraph 0115). However a photo cross-linker -succinimidyl 6-(4-bromomethyl-3-nitrobenzoyl) aminohexanoate was known in the art at the time of the claimed invention as taught by Heckman.

Heckman teaches a photo cross-linker -succinimidyl 6-(4-bromomethyl-3-nitrobenzoyl) aminohexanoate (column 3, lines 15-16) and further teaches that photo-cross linking agent can be incorporated in to an internal nucleotide of the nucleic acid molecule to identify the binding nucleic acid and/or polypeptide partner molecules (column 3, lines 19-67).

It would be obvious to one having the ordinary skill in the art at the time the invention was made to include the a photo cross-linker -succinimidyl 6-(4-bromomethyl-3-nitrobenzoyl) aminohexanoate of Heckman as an additional resource of photo cross linker in the method of O'Donnell with the expected benefit of incorporating photo-cross linker in to an internal nucleotide of the nucleic acid molecule to identify the binding nucleic acid and/or polypeptide partner molecules (column 3, lines 19-67).

Regarding claim 8, O'Donnell in view of Heckman teaches a substrate is a glass substrate (pg. 49, lines 1-5) having a primary amino group formed on the surface (Fig. 7, step 2), a thiol (SH) group is bonded to the terminal of the substance, and the amino group and the thiol group are bonded together by a compound (Fig. 7, step 3) using SIAB linker or succinimidyl 6-(4-bromomethyl-3-nitrobenzoyl) aminohexanoate (Heckman, column 3, lines 15-16) as an alternative source, through a reaction between the amino group and the succinimide ester site of the compound and a reaction between the thiol group and the bromobenzyl site of the compound (Fig. 7, steps 3 and 4; See Example 1, pgs. 68-70).

Regarding claim 9, O'Donnell in view of Heckman teaches the formation of a primary amino group on the glass substrate is carried out by using a silane coupling agent having the primary amino group (Fig. 7, pg. 23, lines 14-19).

Regarding claim 10, O'Donnell in view of Heckman teaches a substrate is a glass substrate (pg. 49, lines 1-5) having a sulfanyl group formed on the surface, an amino group is bonded to the terminal of the substance, and the thiol group and the amino group are bonded together by a compound, that is SIAB linker or succinimidyl 6-(4-bromomethyl-3-nitrobenzoyl) aminohexanoate (Heckman, column 3, lines 15-16) as an alternative source, through a reaction between the thiol group and the bromobenzyl site of the compound and a reaction between the amino group and the succinimide ester site of the compound (Fig. 7, steps 3 and 4; See Example 1, pgs. 68-70).

Regarding claim 11, O'Donnell in view of Heckman teaches the formation of a thiol group on the glass substrate is carried out by using a silane coupling agent having the thiol group (pg. 65, lines 11-13).

Claim 31 is dependent on claim 27. Claim 32 is dependent on claim 31, which is dependent on claim 27. Claim 33 is dependent on claim 32, which is dependent on claim 31, which is dependent on claim 27. Claim 34 is dependent on claim 31, which is dependent on claim 27. Claim 35 is dependent on claim 34, which is dependent on claim 31, which is dependent on claim 27.

Teachings of O'Donnell regarding claim 27 are described previously in this office action on pages 6-8.

Regarding claim 31, O'Donnell teaches an exemplary photocleavable cross-linker include but are not limited to, 3-amino-(2-nitrophenyl) propionic acid (pg. 33, line 15, pgs. 38-47) but do not teach specifically a photo cross linker containing a nitrobenzene derivative- succinimidyl 6-(4-bromomethyl-3-nitrobenzoyl) aminohexanoate (see instant specification paragraph 0115). However a photo cross-linker -succinimidyl 6-(4-bromomethyl-3-nitrobenzoyl) aminohexanoate was known in the art at the time of the claimed invention as taught by Heckman.

Heckman teaches a photo cross-linker -succinimidyl 6-(4-bromomethyl-3-nitrobenzoyl) aminohexanoate (column 3, lines 15-16) and further teaches that photo-cross linking agent can be incorporated in to an internal nucleotide of the nucleic acid

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molecule to identify the binding nucleic acid and/or polypeptide partner molecules (column 3, lines 19-67).

It would be obvious to one having the ordinary skill in the art at the time the invention was made to include the a photo cross-linker -succinimidyl 6-(4-bromomethyl-3-nitrobenzoyl) aminohexanoate of Heckman as an additional resource of photo cross linker in the method of O'Donnell with the expected benefit of incorporating photo-cross linker in to an internal nucleotide of the nucleic acid molecule to identify the binding nucleic acid and/or polypeptide partner molecules (column 3, lines 19-67).

Regarding claim 32, O'Donnell in view of Heckman teaches a substrate is a glass substrate (pg. 49, lines 1-5) on which primary amino group is formed (Fig. 7, pg. 23, lines 14-19) having a sulfanil group is bonded to a 5'- terminal of the primer (Fig. 7, pg. 32 lines 11-15) and the amino group is bonded to the sulfanil group via a compound, that is SIAB linker or succinimidyl 6-(4-bromomethyl-3-nitrobenzoyl) aminohexanoate (Heckman, column 3, lines 15-16) as an alternative source, through a reaction between the thiol group and the bromobenzyl site of the compound and a reaction between the amino group and the succinimide ester site of the compound (Fig. 7, steps 3 and 4; See Example 1, pgs. 68-70).

Regarding claim 33, O'Donnell in view of Heckman teaches the formation of a primary amino group on the glass substrate is carried out by using a silane coupling agent having the primary amino group (Fig. 7, pg. 23, lines 14-19).

Regarding claim 34, O'Donnell in view of Heckman teaches a substrate is a glass substrate (pg. 49, lines 1-5) having a sulfanil group formed on the surface, an amino group is bonded to the terminal of the substance, and the thiol group and the amino group are bonded together by a compound, that is SIAB linker or succinimidyl 6-(4-bromomethyl-3-nitrobenzoyl) aminohexanoate (Heckman, column 3, lines 15-16) as an alternative source, through a reaction between the thiol group and the bromobenzyl site of the compound and a reaction between the amino group and the succinimide ester site of the compound (Fig. 7, steps 3 and 4; See Example 1, pgs. 68-70).

Regarding claim 35, O'Donnell in view of Heckman teaches that a sulfanil group is formed on the glass substrate by using a silane coupling agent having a sulfanil group (Fig. 7, last step).

O'Donnell teaches further that attachment of nucleic acids using silane and photocleavable reagent attached to the glass support is very useful for producing spatially addressable arrays of nucleic acids (pg. 65, lines 5-29) which can be further used for diagnostic methods based on nucleic acid detection and polymorphism analysis (pg. 67, lines 5-11).

It would be obvious to one having the ordinary skill in the art at the time the invention was made to include the method of attaching nucleic acids using silane and photocleavable reagent the glass support of O'Donnell in the method of O'Donnell in view of Heckman with the expected benefit of producing spatially addressable arrays of nucleic acids (pg. 65, lines 5-29) which can be further used for diagnostic methods

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based on nucleic acid detection and polymorphism analysis as taught by O'Donnell (pg. 67, lines 5-11).

### **Conclusion**

10. No claim is allowed

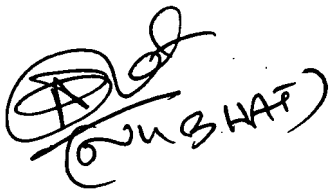
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Narayan K. Bhat whose telephone number is (571)-272-5540. The examiner can normally be reached on 8.30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram R. Shukla can be reached on (571)-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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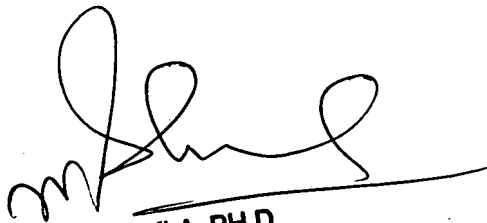
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Handwritten signature of Narayan K. Bhat, with the name "NARAYAN K. BHAT" written in capital letters below the signature.

Narayan K. Bhat Ph. D.

Examiner

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Handwritten signature of Ram R. Shukla, with the name "RAM R. SHUKLA, PH.D." and the title "SUPERVISORY PATENT EXAMINER" printed in capital letters below the signature.RAM R. SHUKLA, PH.D.  
SUPERVISORY PATENT EXAMINER